SYNGAP1-Related Syndrome

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This guide is not meant to take the place of medical advice.

Please consult with your doctor about your genetic results and health care choices. The information in this guide was up to date at the time it was written in 2019. But new information may come to light with new research. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has SYNGAP1-related syndrome.

What is SYNGAP1-related syndrome?

SYNGAP1-related syndrome happens when there are changes to the SYNGAP1 gene. These changes can keep the gene from working as it should.

Key role

The SYNGAP1 gene plays a key role in the development and function of the brain. It makes a protein that helps to control brain activity. When one copy of the SYNGAP1 gene is not working properly, the brain may become overactive.

Symptoms

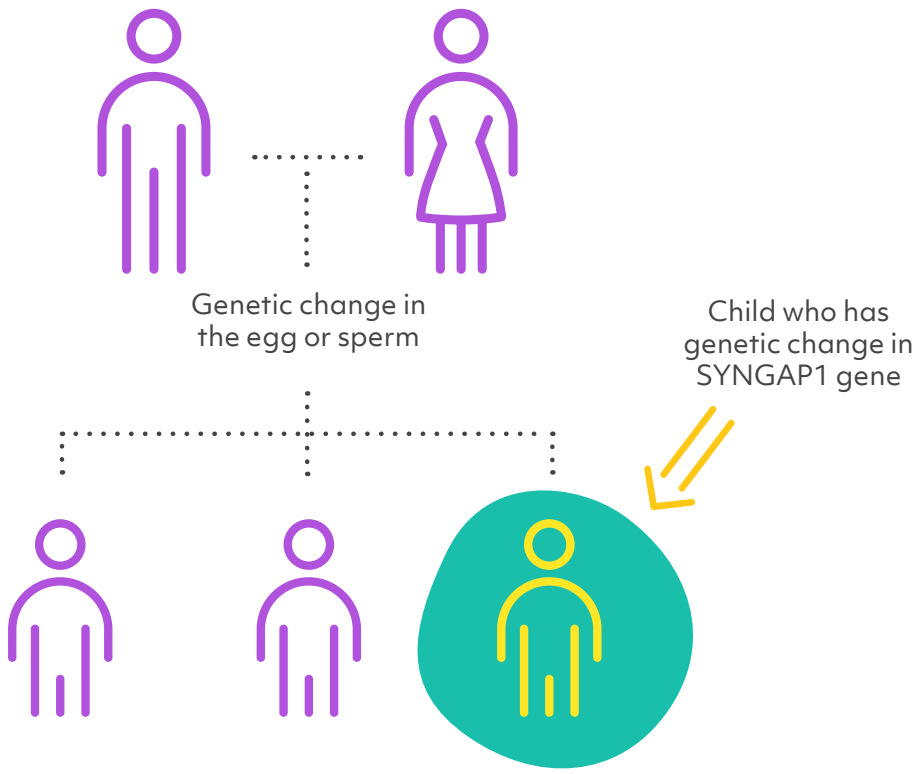
Because the SYNGAP1 gene controls brain activity, changes in this gene can be linked to seizures and other challenges. SYNGAP1-related syndrome can affect the development of communication, social, and learning skills. Many people who have SYNGAP1-related syndrome have:

- Developmental delay, or intellectual disability, or both
- Hyperactivity and sleep problems
- Autism or features of autism
- Seizures
- Joint and spine issues
- Low muscle tone
- Constipation

What causes SYNGAP1-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the SYNGAP1 gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. In most cases, parents pass on exact copies of the gene to their child. But the process of copying genes is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

Sometimes a random change happens in the sperm or egg. This change to the genetic code is called a 'de novo', or new, change. The child can be the first in the family to have the gene change.



De novo changes can take place in any gene. We all have some de novo changes, most of which don't affect our health. But because SYNGAP1 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that SYNGAP1-related syndrome is often the result of a de novo change in SYNGAP1. Many parents who have had their genes tested do not have the SYNGAP1 gene change found in their child. In some cases, SYNGAP1-related syndrome happens because the gene change was passed down from a parent.

Our genes are arranged in long threads called chromosomes. The SYNGAP1 gene is located on chromosome 6. Some people who are missing parts of chromosome 6, including the entire SYNGAP1 gene, have symptoms similar to people who have changes in the SYNGAP1 gene.

Why does my child have a change in the SYNGAP1 gene?

No parent causes their child's SYNGAP1-related syndrome. We know this because no parent has any control over the gene changes that they do or do not pass on to their children. Please keep in mind that nothing a parent does before or during the pregnancy causes this to happen. The gene change takes place on its own and cannot be predicted or stopped.

What are the chances that other family members or future children will have SYNGAP1-related syndrome?

Each family is different. A geneticist or genetic counselor can give you advice on the chance that this will happen again in your family.

The risk of having another child who has SYNGAP1-related syndrome depends on the genes of both birth parents.

- If neither birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is on average 1 percent. This 1 percent chance is higher than the chance of the general population. The increase in risk is due to the very unlikely chance that more of the mother's egg cells or the father's sperm cells carry the same change in the gene.
- If one birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has SYNGAP1-related syndrome, the risk of having a child who has the syndrome depends on the symptom-free sibling's genes and their parents' genes.

- If neither parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child who has SYNGAP1-related syndrome.
- If one birth parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a small chance of also having the same gene change. If the symptom-free sibling has the same gene change as their sibling who has the syndrome, the symptom-free sibling's chance of having a child who has SYNGAP1-related syndrome is 50 percent.

For a person who has SYNGAP1-related syndrome, the risk of having a child who has the syndrome is about 50 percent.

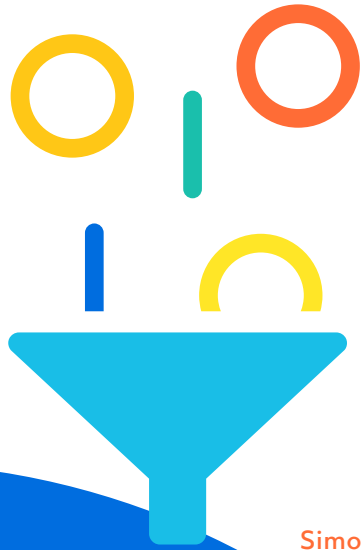
How many people have SYNGAP1-related syndrome?

As of 2017, doctors had found about 85 people in the world with changes in the SYNGAP1 gene. The first case of SYNGAP1-related syndrome was described in 2015. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have SYNGAP1-related syndrome look different?

People who have SYNGAP1-related syndrome do not look very different. Appearance can vary and can include some but not all of these features:

- Broad nasal bridge
- Long nose
- Full lower lip



How is SYNGAP1-related syndrome treated?

Scientists and doctors have only just begun to study SYNGAP1-related syndrome. At this point, there are no medicines designed to treat the syndrome. A genetic diagnosis can help people decide on the best way to track the condition and manage therapies. Doctors can refer people to specialists for:

- Physical exams and brain studies
- Genetics consults
- Development and behavior studies
- Other issues, as needed

A developmental pediatrician, neurologist, or psychologist can follow progress over time and can help:

- Suggest the right therapies. This can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for SYNGAP1-related syndrome should begin as early as possible, ideally before a child begins school.

If seizures happen, consult a neurologist. There are many different types of seizures, and not all types are easy to spot. To learn more, you can refer to resources such as the Epilepsy Foundation's website: epilepsy.com/learn/types-seizures.

SYNGAP1-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2017, studies found around 85 people who have SYNGAP1-related syndrome.

This section includes a summary of information from major published articles. It highlights how many people have different symptoms. To learn more about the articles, see the Sources and references section of this guide.

Behavior and development concerns linked to SYNGAP1-related syndrome

Speech

Almost all children who have SYNGAP1-related syndrome have speech delay. Children are often late to start talking and may have limited vocabulary.

Learning

Most children who have SYNGAP1-related syndrome show some degree of intellectual disability, ranging from mild to severe. They need special educational support.

Behavior

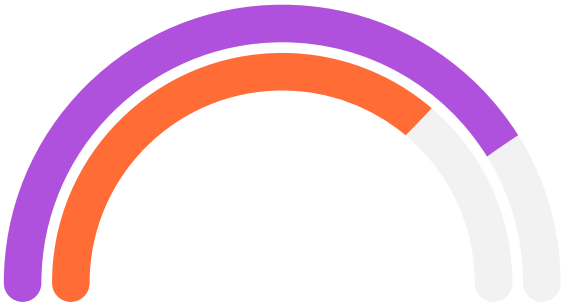
Some people who have SYNGAP1-related syndrome have aggressive or challenging behaviors and sleep problems.

Medical and physical concerns linked to SYNGAP1-related syndrome

A study of 10 people who have SYNGAP1-related syndrome found these symptoms:

Brain and muscle tone

Low muscle tone, also called hypotonia, can cause delays in developmental milestones, such as sitting and walking, as well as a wide-based or unsteady walk.



8 out of 10 had low muscle tone

7 out of 10 had epilepsy

Feeding and digestion issues

5 out of 10 had constipation

Facial features

Some people who have SYNGAP1-related syndrome have distinct facial features, such as a broad nasal bridge, a long nose, and a full lower lip.

Eyes

3 out of 10 people had crossed eyes, also called strabismus.

Joints

2 out of 10 people had problems with the hip socket, also called hip dysplasia.

- **Simons Searchlight Community SYNGAP1 Facebook group**
  www.facebook.com/groups/SYNGAP1

- **Bridge the Gap—SYNGAP—Education & Research Foundation**
  www.bridgesyngap.org

- **SynGap Research Fund Foundation**
  www.syngapresearchfund.org

Sources and References

The content in this guide comes from published studies about SYNGAP1-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

- Parker MJ. *et al. American Journal of Medical Genetics Part A*, **167A**, 2231-2237, (2015). De novo, heterozygous, loss-of-function mutations in SYNGAP1 cause a syndromic form of intellectual disability
  www.ncbi.nlm.nih.gov/pubmed/26079862

- Mignot C. *et al. Journal of Medical Genetics*, **53**, 511-522, (2016). Genetic and neurodevelopmental spectrum of SYNGAP1-associated intellectual disability and epilepsy
  www.ncbi.nlm.nih.gov/pubmed/26989088

- Prchalova D. *et al. BMC Medical Genetics*, **18**, 62, (2017). Analysis of 31-year-old patient with SYNGAP1 gene defect points to importance of variants in broader splice regions and reveals developmental trajectory of SYNGAP1-associated phenotype
  www.ncbi.nlm.nih.gov/pubmed/28576131

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